



## General

### Guideline Title

Diagnosis and treatment of polycystic ovary syndrome: an Endocrine Society clinical practice guideline.

### Bibliographic Source(s)

Legro RS, Arslanian SA, Ehrmann DA, Hoeger KM, Murad MH, Pasquali R, Welt CK. Diagnosis and treatment of polycystic ovary syndrome: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2013 Dec;98(12):4565-92. [PubMed](#)

### Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

## Regulatory Alert

### FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- [April 8, 2016 – Metformin-containing Drugs](#) : The U.S. Food and Drug Administration (FDA) is requiring labeling changes regarding the recommendations for metformin-containing medicines for diabetes to expand metformin's use in certain patients with reduced kidney function. The current labeling strongly recommends against use of metformin in some patients whose kidneys do not work normally. FDA concluded, from the review of studies published in the medical literature, that metformin can be used safely in patients with mild impairment in kidney function and in some patients with moderate impairment in kidney function.

## Recommendations

### Major Recommendations

Definitions for the quality of the evidence (+OOO, ++OO, +++O, and ++++); the strength of the recommendation (1 or 2); and the difference between a "recommendation" and a "suggestion" are provided at the end of the "Major Recommendations" field.

Diagnosis of Polycystic Ovary Syndrome (PCOS)

## Diagnosis in Adults

The Task Force suggests that the diagnosis of PCOS be made if two of the three following criteria are met: androgen excess, ovulatory dysfunction, or polycystic ovaries (PCO) (see Tables 1 and 2 in the original guideline document), whereas disorders that mimic the clinical features of PCOS are excluded. These include, in all women: thyroid disease, hyperprolactinemia, and nonclassic congenital adrenal hyperplasia (primarily 21-hydroxylase deficiency by serum 17-hydroxyprogesterone [17-OHP]) (see Table 3 in the original guideline document). In select women with amenorrhea and more severe phenotypes, the Task Force suggests more extensive evaluation excluding other causes (see Table 4 in the original guideline document) (2|+++O).

## Diagnosis in Adolescents

The Task Force suggests that the diagnosis of PCOS in an adolescent girl be made based on the presence of clinical and/or biochemical evidence of hyperandrogenism (after exclusion of other pathologies) in the presence of persistent oligomenorrhea. Anovulatory symptoms and PCO morphology are not sufficient to make a diagnosis in adolescents, as they may be evident in normal stages in reproductive maturation (2|++OO).

## Diagnosis in Perimenopause and Menopause

Although there are currently no diagnostic criteria for PCOS in perimenopausal and menopausal women, the Task Force suggests that a presumptive diagnosis of PCOS can be based upon a well-documented long term history of oligomenorrhea and hyperandrogenism during the reproductive years. The presence of PCO morphology on ultrasound would provide additional supportive evidence, although this is less likely in a menopausal woman (2|++OO).

## Associated Morbidity and Evaluation

### Cutaneous Manifestations

The Task Force recommends that a physical examination should document cutaneous manifestations of PCOS: terminal hair growth (see The Endocrine Society guideline [Evaluation and Treatment of Hirsutism in Premenopausal Women](#) [ ]), acne, alopecia, acanthosis nigricans, and skin tags (1|+++O).

### Infertility

Women with PCOS are at increased risk of anovulation and infertility; in the absence of anovulation, the risk of infertility is uncertain. The Task Force recommends screening ovulatory status using menstrual history in all women with PCOS seeking fertility. Some women with PCOS and a eumenorrheic menstrual history may still experience anovulation and a midluteal serum progesterone may be helpful as an additional screening test (1|++OO).

The Task Force recommends excluding other causes of infertility, beyond anovulation, in couples where a woman has PCOS (1|++OO).

### Pregnancy Complications

Because women with PCOS are at increased risk of pregnancy complications (gestational diabetes, preterm delivery, and pre-eclampsia) exacerbated by obesity, the Task Force recommends preconceptional assessment of body mass index (BMI), blood pressure, and oral glucose tolerance (1|+++O).

### Fetal Origins

The evidence for intrauterine effects on development of PCOS is inconclusive. The Task Force suggests no specific interventions for prevention of PCOS in offspring of women with PCOS (2|+OOO).

### Endometrial Cancer

Women with PCOS share many of the risk factors associated with the development of endometrial cancer including obesity, hyperinsulinism, diabetes, and abnormal uterine bleeding. However, The Task Force suggests against routine ultrasound screening for endometrial thickness in women with PCOS (2|+++O).

### Obesity

Increased adiposity, particularly abdominal, is associated with hyperandrogenemia and increased metabolic risk (see The Endocrine Society guideline [Primary Prevention of Cardiovascular Disease and Type 2 Diabetes in Patients at Metabolic Risk](#) [ ]). Therefore, the Task Force recommends screening adolescents and women with PCOS for increased adiposity, by BMI calculation and measurement of waist

circumference (1|+++O).

## Depression

The Task Force suggests screening women and adolescents with PCOS for depression and anxiety by history and, if identified, providing appropriate referral and/or treatment (2|++OO).

## Sleep-Disordered Breathing/Obstructive Sleep Apnea (OSA)

The Task Force suggests screening overweight/obese adolescents and women with PCOS for symptoms suggestive of OSA and, when identified, obtaining a definitive diagnosis using polysomnography. If OSA is diagnosed, patients should be referred for institution of appropriate treatment (2|++OO).

## Nonalcoholic Fatty Liver Disease (NAFLD) and Nonalcoholic Steatohepatitis (NASH)

The Task Force suggests awareness of the possibility of NAFLD and NASH but recommends against routine screening (2|++OO).

## Type 2 Diabetes Mellitus (T2DM)

The Task Force recommends the use of an oral glucose tolerance test (OGTT) (consisting of a fasting and 2-hour glucose level using a 75-g oral glucose load) to screen for impaired glucose tolerance (IGT) and T2DM in adolescents and adult women with PCOS because they are at high risk for such abnormalities (1|+++O). A hemoglobin A1c (HgbA1c) test may be considered if a patient is unable or unwilling to complete an OGTT (2|++OO). Rescreening is suggested every 3–5 years, or more frequently if clinical factors such as central adiposity, substantial weight gain, and/or symptoms of diabetes develop (2|++OO).

## Cardiovascular Risk

The Task Force recommends that adolescents and women with PCOS be screened for the following cardiovascular disease risk factors (see Table 5 in the original guideline document): family history of early cardiovascular disease, cigarette smoking, IGT/T2DM, hypertension, dyslipidemia, OSA, and obesity (especially increased abdominal adiposity) (1|++OO).

## Treatment

### Hormonal Contraceptives (HCs): Indications and Screening

The Task Force recommends HCs (i.e., oral contraceptives, patch, or vaginal ring) as first-line management for the menstrual abnormalities and hirsutism/acne of PCOS (refer to The Endocrine Society guideline [Evaluation and Treatment of Hirsutism in Premenopausal Women](#) [2014], recommendation 2.1.1), which treat these two problems concurrently (1|++OO).

The Task Force recommends screening for contraindications to HC use via established criteria (see Table 6 in the original guideline document and the National Guideline Clearinghouse summary of the Centers for Disease Control and Prevention's guideline [U.S. medical eligibility criteria for contraceptive use, 2010](#)) (1|++OO). For women with PCOS, the Task Force does not suggest one HC formulation over another (2|+++O).

### Role of Exercise in Lifestyle Therapy

The Task Force suggests the use of exercise therapy in the management of overweight and obesity in PCOS (2|++OO). Although there are no large randomized trials of exercise in PCOS, exercise therapy, alone or in combination with dietary intervention, improves weight loss and reduces cardiovascular risk factors and diabetes risk in the general population.

### Role of Weight Loss in Lifestyle Therapy

The Task Force suggests that weight loss strategies begin with calorie-restricted diets (with no evidence that one type of diet is superior) for adolescents and women with PCOS who are overweight or obese (2|++OO). Weight loss is likely beneficial for both reproductive and metabolic dysfunction in this setting. Weight loss is likely insufficient as a treatment for PCOS in normal-weight women.

### Use of Metformin

The Task Force suggests against the use of metformin as a first-line treatment of cutaneous manifestations, for prevention of pregnancy complications, or for the treatment of obesity (2|++OO).

The Task Force recommends metformin in women with PCOS who have T2DM or IGT who fail lifestyle modification (1|+++O). For women with PCOS with menstrual irregularity who cannot take or do not tolerate HCs, The Task Force suggests metformin as second-line therapy (2|+++O).

## Treatment of Infertility

The Task Force recommends clomiphene citrate (or comparable estrogen modulators such as letrozole) as the first-line treatment of anovulatory infertility in women with PCOS (1|+++O).

The Task Force suggests the use of metformin as an adjuvant therapy for infertility to prevent ovarian hyperstimulation syndrome (OHSS) in women with PCOS undergoing in vitro fertilization (IVF) (2|++OO).

## Use of Other Drugs

The Task Force recommends against the use of insulin sensitizers, such as inositols (due to lack of benefit) or thiazolidinediones (given safety concerns), for the treatment of PCOS (1|+++O).

The Task Force suggests against the use of statins for treatment of hyperandrogenism and anovulation in PCOS until additional studies demonstrate a favorable risk-benefit ratio (2|++OO). However, The Task Force suggests statins in women with PCOS who meet current indications for statin therapy (2|++OO).

## Treatment of Adolescents

The Task Force suggests HCs as the first-line treatment in adolescents with suspected PCOS (if the therapeutic goal is to treat acne, hirsutism, or anovulatory symptoms, or to prevent pregnancy) (2|++OO). The Task Force suggests that lifestyle therapy (calorie-restricted diet and exercise) with the objective of weight loss should also be first-line treatment in the presence of overweight/obesity (2|++OO). The Task Force suggests metformin as a possible treatment if the goal is to treat IGT/metabolic syndrome (2|++OO). The optimal duration of HC or metformin use has not yet been determined.

For premenarchal girls with clinical and biochemical evidence of hyperandrogenism in the presence of advanced pubertal development (i.e.,  $\geq$  Tanner stage IV breast development), the Task Force suggests starting HCs (2|++OO).

## Definitions:

### Quality of Evidence

+OOO Denotes very low quality evidence

++OO Denotes low quality evidence

+++O Denotes moderate quality evidence

++++ Denotes high quality evidence

### Strength of Recommendation

1 - Indicates a strong recommendation and is associated with the phrase "The Task Force recommends."

2 - Denotes a weak recommendation and is associated with the phrase "The Task Force suggests."

## Clinical Algorithm(s)

None provided

## Scope

### Disease/Condition(s)

Polycystic ovary syndrome (PCOS)

### Guideline Category

Diagnosis

Evaluation

Management

Risk Assessment

Screening

Treatment

## Clinical Specialty

Dermatology

Endocrinology

Family Practice

Internal Medicine

Obstetrics and Gynecology

Pediatrics

## Intended Users

Advanced Practice Nurses

Physician Assistants

Physicians

## Guideline Objective(s)

To formulate practice guidelines for the diagnosis and treatment of polycystic ovary syndrome (PCOS)

## Target Population

Adolescents and adults with known or suspected polycystic ovary syndrome (PCOS)

## Interventions and Practices Considered

Diagnosis/Evaluation

Diagnosis of polycystic ovary syndrome (PCOS) in adults based on androgen excess, ovulatory dysfunction, or polycystic ovaries (PCO) and exclusion of other causes

Diagnosis of PCOS in adolescents based on the presence of clinical and/or biochemical evidence of hyperandrogenism (after exclusion of other pathologies) in the presence of persistent oligomenorrhea

Diagnosis in perimenopause and menopause based upon a well-documented long term history of oligomenorrhea and hyperandrogenism during the reproductive years, presence of PCO morphology on ultrasound

Evaluation of associated morbidity

- Evaluation of cutaneous manifestations (terminal hair growth, acne, alopecia, acanthosis nigricans, and skin tags)
- Evaluation for infertility: screening ovulatory status using menstrual history, midluteal serum progesterone
- Risk assessment for pregnancy complications: preconceptional assessment of body mass index (BMI), blood pressure, and oral

glucose tolerance

- Screening for obesity: BMI calculation and measurement of waist circumference
- Screening for depression and anxiety and referral for treatment
- Screening for sleep-disordered breathing/obstructive sleep apnea (OSA) and referral for treatment
- Screening for type 2 diabetes mellitus (T2DM): use of an oral glucose tolerance test (OGTT) or hemoglobin A1c (HgbA1c) test
- Screening for cardiovascular disease risk factors

## Management/Treatment

1. Hormonal contraceptives (HCs; oral contraceptives, patch, or vaginal ring) as first-line management for menstrual abnormalities and hirsutism/acne
2. Screening for contraindications to hormonal contraceptives using established criteria
3. Lifestyle therapy: exercise and weight loss
4. Metformin (recommendation against use as first-line treatment of cutaneous manifestations, for prevention of pregnancy complications, or for the treatment of obesity)
5. Treatment of infertility: clomiphene citrate (or comparable estrogen modulators such as letrozole)
6. Statins in women with PCOS who meet current indications for statin therapy
7. Considerations for treatment of adolescents and premenarchal girls

Note: The following were considered but not recommended or no specific recommendation was made: prevention of PCOS in offspring of women with PCOS, routine ultrasound screening for endometrial thickness, routine screening for nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH), statins for treatment of hyperandrogenism and anovulation in PCOS, insulin sensitizers, such as inositols, or thiazolidinediones for the treatment of PCOS.

## Major Outcomes Considered

- Risk for lactic acidosis in patients taking metformin
- Thromboembolic events (venous or arterial) in patients taking oral contraceptives
- Other cardiovascular events
- Overall cancer risk
- Incidence of diabetes
- Changes in weight and body mass index (BMI)
- Antiandrogen-induced liver injury
- Metabolic parameters such as:
  - Blood glucose (fasting blood glucose, postprandial glucose, glucose tolerance test, random glucose, and area under the curve of glucose)
  - Insulin resistance (as glucose-to-insulin ratio, Homeostasis Model of Assessment of Insulin Resistance, Quantitative Insulin Sensitivity Check Index)
- Hirsutism score
- Fertility
- Amenorrhea
- Acne
- Pregnancy rate

## Methodology

### Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

## Description of Methods Used to Collect/Select the Evidence

The Endocrine Society's Task Force commissioned two systematic reviews (see the "Availability of Companion Documents" field) to support the guideline.

### Adverse Effects of the Common Treatments for Polycystic Ovary Syndrome: A Systematic Review and Meta-Analysis

#### Eligibility Criteria

The reviewers sought to include randomized controlled trials (RCTs) and comparative observational studies enrolling women with polycystic ovary syndrome (PCOS) who received metformin (Mt), oral contraceptive pills (OCPs), or antiandrogen agents (AAs) for at least 6 months and reported any severe adverse effects. Studies had to include a comparison group of women who had PCOS but received placebo or no treatment.

#### Search Methods

An expert reference librarian, following the protocol, designed and conducted an electronic search strategy (Supplemental Table 1, published on [The Endocrine Society's Journals Online web site](#) ). Ovid Medline, OVID EMBASE, OVID Cochrane Library, Web of Science, Scopus, PsycINFO, and CINAHL were searched from inception through April 2011, without language limitations. To identify additional candidate studies, the reference lists of the eligible primary studies, narrative reviews, and systematic reviews were reviewed, and the expert members of the commissioning task force were queried.

#### Study Selection

Two reviewers working independently considered the potential eligibility of each of the abstracts and titles that result from executing the search strategy. Eligible studies were reviewed in full text version. Disagreements were resolved by consensus.

### Lifestyle Modification Programs in Polycystic Ovary Syndrome: Systematic Review and Meta-Analysis

#### Eligibility Criteria

Reviewers included RCTs that enrolled woman of any age with PCOS who received lifestyle modifications (LSM), broadly comprising modifications of diet and/or physical activity, and compared them against women who had the same diagnosis but received metformin, the most commonly used agent in PCOS or minimal intervention (MI), which could be a control or placebo intervention.

#### Search Methods

An expert reference librarian, following the protocol, designed and conducted an electronic search strategy (Supplemental Table 1, published on [The Endocrine Society's Journals Online web site](#) ). Electronic databases were searched to identify relevant studies (Ovid Medline, OVID EMBASE, OVID Cochrane Library, Web of Science, Scopus, PsycINFO, and CINAHL) through January 2011. To identify additional candidate studies, the reference lists of the eligible primary studies, narrative reviews, and systematic reviews were reviewed, and the expert members of the commissioning task force were queried.

#### Selection of Studies

Two reviewers working independently considered the potential eligibility of each of the abstracts and titles that result from executing the search strategy. Eligible studies were reviewed in full-text versions (all available versions of each study). There were no disagreements between the reviewers in the full text screening.

## Number of Source Documents

### Adverse Effects of the Common Treatments for Polycystic Ovary Syndrome: A Systematic Review and Meta-Analysis

Literature search identified 1076 potentially eligible articles, of which 22 original studies reported in 25 publications, enrolling 1335 polycystic ovary syndrome (PCOS) patients, met the eligibility criteria and were included in the direct evidence part of the systematic review.

### Lifestyle Modification Programs in Polycystic Ovary Syndrome: Systematic Review and Meta-Analysis

A literature search identified 745 articles of which 9 randomized control trials (RCT) in 10 publications were eligible.

# Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

## Rating Scheme for the Strength of the Evidence

Quality of Evidence

+OOO Denotes very low quality evidence

++OO Denotes low quality evidence

+++O Denotes moderate quality evidence

++++ Denotes high quality evidence

## Methods Used to Analyze the Evidence

Meta-Analysis

Meta-Analysis of Randomized Controlled Trials

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

## Description of the Methods Used to Analyze the Evidence

The Endocrine Society's Task Force commissioned two systematic reviews (see the "Availability of Companion Documents" field) to support the guideline.

Adverse Effects of the Common Treatments for Polycystic Ovary Syndrome: A Systematic Review and Meta-Analysis

Data Extraction and Management

Using a standardized, piloted, and web-based data extraction form and working in duplicate, reviewers abstracted the following descriptive data from each study: full description of participants enrolled (principal baseline characteristics as age, childbearing, weight and body mass index [BMI]), the interventions they received (type, dose, and frequency), the control interventions, the monitoring for efficacy or adherence, the measure of outcome (specifically defined as event or measure and timeframe for the ascertainment of this outcome), and the source of funding. The outcomes of interest were extracted at the longest point of complete follow-up.

Outcomes of Interest

The outcomes of interest were 1) for metformin lactic acidosis; 2) for oral contraceptive pills (OCPs) thromboembolic events (venous or arterial) and other cardiovascular events, overall cancer risk, incidence of diabetes, changes in weight and BMI; and 3) for antiandrogen agents drug-induced liver injury. Metabolic parameters such as blood glucose (fasting blood glucose, postprandial glucose, glucose tolerance test, random glucose, and area under the curve of glucose) and insulin resistance (as glucose-to-insulin ratio, Homeostasis Model of Assessment of Insulin Resistance, Quantitative Insulin Sensitivity Check Index) were extracted and analyzed for antiandrogen agents and OCPs only. The gastrointestinal side effects of metformin were not evaluated because these patients often abandon therapy promptly and would be underrepresented in the long-term studies reviewers sought to include.

Author Contact

The reviewers contacted authors of studies in which data were not available or were reported incompletely for review purposes. They used a maximum of two contacts via e-mail, or by postal mail if e-mail was not available, at 2-week intervals.

Assessment of Risk of Bias in Individual Included Studies

To assess the methodological quality of the included randomized control trials (RCTs) the Cochrane risk of bias assessment tool was used to



evaluate randomization performance and methods, allocation concealment, baseline imbalances, extent of blinding (patients, caregivers, data collectors, outcome assessors, and data analysts), rate of loss to follow-up, and whether adherence was monitored. For observational studies the Newcastle and Ottawa quality assessment tool was used to evaluate how the groups were selected, the comparability between them, whether there was adequate follow-up, and how outcomes/exposure were ascertained.

#### Meta-Analysis

For dichotomous outcomes the risk ratio was estimated and for continuous outcomes the weighted mean difference (WMD) was estimated. Random-effects model was chosen a priori to pool effect size across studies. The  $I^2$  statistic was used to measure inconsistency in results across studies. The  $I^2$  statistic quantifies differences in results between studies that are not attributable to chance, therefore reflecting true inconsistency between different trials. Analyses were performed using Comprehensive Meta-Analysis version 2.2 (BioStat Inc). Analysis was conducted separately in pregnant and nonpregnant women.

#### Indirect Evidence

Anticipating sparse adverse effect data in studies of women with polycystic ovary syndrome (PCOS), the reviewers planned to present the best available evidence simultaneously about adverse effects of the interventions of choice in patients without PCOS (patients with diabetes, healthy women, and women with hirsutism). This indirect evidence may be extrapolated to women with PCOS. The reviewers searched for systematic reviews and, if not available, for studies with long-term follow-up as a representative sample of indirect evidence of the adverse effects of the drugs of interest. These data are presented separately as indirect evidence.

#### Subgroup and Sensitivity Analysis

The reviewers determined a priori a limited number of hypotheses to explore subgroups interactions and potential explanations for inconsistency. Subgroup analyses were based on 1) syndrome severity; 2) methodological quality; 3) patient's baseline weight (overweight vs non-overweight); 4) daily dose of the medications; 5) length of the intervention. The reviewers planned to test the hypotheses of a subgroup effect using a test of interaction and to conduct meta-regression to assess the correlation between the effect size and doses of drugs.

#### Lifestyle Modification Programs in Polycystic Ovary Syndrome: Systematic Review and Meta-Analysis

#### Data Extraction and Management

Using a standardized, piloted, and web-based data extraction form and working in duplicates, reviewers abstracted the following descriptive data from each study: full descriptions of participants enrolled (principal baseline characteristics such as age, childbearing, weight, and BMI), the interventions they received (type and frequency), the control interventions, the monitoring for efficacy of the follow-up and adherence to the treatment, the measure of outcome (specifically defined as an event or measure and time frame for the ascertainment of this outcome) and the source of funding. The outcomes of interest were extracted at the longest point of complete follow-up.

#### Author Contact

When data were not available from the published articles, repeated efforts were made to contact the authors. The reviewers decided a priori to attempt a maximum of 2 times per each author (through e-mail), with 2 weeks between each attempt. When the author's e-mail address was not available, the contacts were made by mail.

#### Assessment of Risk of Bias in Included Studies

To assess the methodological quality of the included RCTs, the Cochrane risk of bias assessment tool was used to evaluate randomization performance and methods, allocation concealment, baseline imbalances, extent of blinding (patients, caregivers, data collectors, outcome assessors, and data analysts), rate of loss to follow-up, and monitoring of adherence.

#### Meta-Analysis

For dichotomous outcomes the odds ratio (OR) was estimated, and for continuous outcomes the WMD was estimated. The  $I^2$  statistic was used to measure inconsistency in results across studies not attributable to chance. To pool data across studies, reviewers tested random-effects and fixed-effects models and present results for both. When the  $I^2$  statistic is 0 (i.e., there is no heterogeneity), the 2 models converge, and data are presented only for 1 model. The random-effects model offers the advantage of incorporating within-study and between-study variances, whereas the fixed-effects model provides more reliable estimates of between-study variance when the number of included studies is small. The analyses were performed using Comprehensive Meta-Analysis (version 2.2; BioStat Inc.).

## Assessment of Publication Bias

Evaluation of publication bias was not feasible because of heterogeneity and the small number of included studies.

## Subgroup Analysis, Meta-Regression, and Sensitivity Analysis

The reviewers determined a priori hypotheses (limited to a small number to avoid chance findings) to explore subgroup interactions and give a potential explanation for heterogeneity. Subgroup analyses were based on (1) patients: baseline BMI (<30 vs >30 kg/m<sup>2</sup>); (2) interventions: physical exercise vs diet vs combined strategies; (3) study quality (good to moderate vs fair to poor); and (4) achieved weight reduction vs no weight reduction achieved. A test of interaction was conducted to evaluate the significance of subgroup analyses and potential correlation between subgroups and the pooled effect size. A meta-regression was also performed to assess the correlation between BMI reduction (independent variable) and metabolic parameters (dependent variable). Reviewers tested every outcome in sensitivity analysis to determine the extent to which the choice of meta-analytic model (fixed effect vs random effects) affects the inferences of each result.

## Methods Used to Formulate the Recommendations

### Expert Consensus

## Description of Methods Used to Formulate the Recommendations

### Participants

An Endocrine Society-appointed Task Force of experts, a methodologist, and a medical writer developed the guideline.

### Evidence

This evidence-based guideline was developed using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) system to describe both the strength of recommendations and the quality of evidence.

### Consensus Process

One group meeting, several conference calls, and e-mail communications enabled consensus. Committees and members of the Endocrine Society and the European Society of Endocrinology reviewed and commented on preliminary drafts of these guidelines. Two systematic reviews (see the "Availability of Companion Documents" field) were conducted to summarize supporting evidence.

## Rating Scheme for the Strength of the Recommendations

### Strength of Recommendation

1 - Indicates a strong recommendation and is associated with the phrase "The Task Force recommends."

2 - Denotes a weak recommendation and is associated with the phrase "The Task Force suggests."

## Cost Analysis

A cost analysis was not performed and published cost analyses were not reviewed.

## Method of Guideline Validation

### External Peer Review

### Internal Peer Review

## Description of Method of Guideline Validation

The Endocrine Society Clinical Guidelines Subcommittee and Clinical Affairs Core Committee provided careful critical review of earlier versions of this manuscript and helpful comments and suggestions. The members of the Endocrine Society kindly reviewed the draft version of this manuscript when it was posted on the Society's website and sent additional comments and suggestions.

## Evidence Supporting the Recommendations

### Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

## Benefits/Harms of Implementing the Guideline Recommendations

### Potential Benefits

Appropriate diagnosis and treatment of polycystic ovary syndrome (PCOS)

### Potential Harms

- There are potential serious side effects to statins (myopathy and renal impairment), which may be more common in women than men, and these drugs are theoretically teratogenic (Pregnancy Category X), which merits caution in their use. Until additional studies demonstrate a clear risk-benefit ratio favoring statin therapy for other aspects of polycystic ovary syndrome (PCOS), statins should only be used in women with PCOS who meet current indications for statin treatment.
- Metformin has the potential for serious side effects, including gastrointestinal disturbance.
- There are insufficient data about whether women with PCOS face increased risk of thromboembolism on particular hormonal contraceptive (HC) preparations, although preparations may vary with respect to thromboembolic risk in the general population. See Table 6 in the original guideline document, which outlines conditions with theoretical or proven risks for HC use.
- More information on potential harms of treatment can be found in "Adverse Effects of the Common Treatments for Polycystic Ovary Syndrome: A Systematic Review and Meta-Analysis" (see the "Availability of Companion Documents" field).

## Contraindications

### Contraindications

See Table 6 in the original guideline document, which outlines conditions with theoretical or proven risks for hormonal contraceptive (HC) use.

## Qualifying Statements

### Qualifying Statements

- Clinical Practice Guidelines are developed to be of assistance to endocrinologists and other health care professionals by providing guidance and recommendations for particular areas of practice. The Guidelines should not be considered inclusive of all proper approaches or methods, or exclusive of others. The Guidelines cannot guarantee any specific outcome, nor do they establish a standard of care. The Guidelines are not intended to dictate the treatment of a particular patient. Treatment decisions must be made based on the independent judgment of health care providers and each patient's individual circumstances.
- The Endocrine Society makes no warranty, express or implied, regarding the Guidelines and specifically excludes any warranties of merchantability and fitness for a particular use or purpose. The Society shall not be liable for direct, indirect, special, incidental, or

## Implementation of the Guideline

### Description of Implementation Strategy

An implementation strategy was not provided.

### Implementation Tools

Patient Resources

Staff Training/Competency Material

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

## Institute of Medicine (IOM) National Healthcare Quality Report Categories

### IOM Care Need

Getting Better

Living with Illness

### IOM Domain

Effectiveness

Patient-centeredness

## Identifying Information and Availability

### Bibliographic Source(s)

Legro RS, Arslanian SA, Ehrmann DA, Hoeger KM, Murad MH, Pasquali R, Welt CK. Diagnosis and treatment of polycystic ovary syndrome: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. 2013 Dec;98(12):4565-92. [PubMed](#)

### Adaptation

Not applicable: The guideline was not adapted from another source.

### Date Released

2013 Dec

## Guideline Developer(s)

The Endocrine Society - Professional Association

## Source(s) of Funding

The Endocrine Society

## Guideline Committee

The Polycystic Ovary Syndrome (PCOS) Guidelines Task Force

## Composition of Group That Authored the Guideline

*Task Force Members:* Richard S. Legro, Silva A. Arslanian, David A. Ehrmann, Kathleen M. Hoeger, M. Hassan Murad, Renato Pasquali, and Corrine K. Welt

## Financial Disclosures/Conflicts of Interest

The Endocrine Society maintains a rigorous conflict of interest review process for the development of clinical practice guidelines. All Task Force members must declare any potential conflicts of interest, which are reviewed before they are approved to serve on the Task Force and periodically during the development of the guideline. The conflict of interest forms are vetted by the Clinical Guidelines Subcommittee (CGS) before the members are approved by the Society's Council to participate on the guideline Task Force. Participants in the guideline development must include a majority of individuals without conflict of interest in the matter under study. Participants with conflicts of interest may participate in the development of the guideline, but they must have disclosed all conflicts. The CGS and the Task Force have reviewed all disclosures for this guideline and resolved or managed all identified conflicts of interest.

Conflicts of interest are defined by remuneration in any amount from the commercial interest(s) in the form of grants; research support; consulting fees; salary; ownership interest (e.g., stocks, stock options, or ownership interest excluding diversified mutual funds); honoraria or other payments for participation in speakers' bureaus, advisory boards, or boards of directors; or other financial benefits. Completed forms are available through the Endocrine Society office.

### Financial Disclosure of Task Force

Silva A. Arslanian, MD is on the advisory board for Sanofi-Aventis, Novo Nordisk and Bristol-Myers Squibb. She is a consultant for GILEAD and Boehringer Ingelheim.

David A. Ehrmann, MD is on the advisory board for Astra-Zeneca.

Corrine K. Welt, MD is a consultant for Astra-Zeneca.

Richard S. Legro, MD (chair), M. Hassan Murad, MD, Kathleen M. Hoeger, and Renato Pasquali, MD have no relevant financial relationships to declare.

## Guideline Endorser(s)

European Society of Endocrinology - Medical Specialty Society

## Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

## Guideline Availability

Electronic copies: Available from [The Endocrine Society Web site](#) .

Print copies: Available from The Endocrine Society, Phone: (301) 941.0210; Email: [SocietyServices@endo-society.org](mailto:SocietyServices@endo-society.org)

## Availability of Companion Documents

The following are available:

- Domecq JP, Prutsky G, Mullan RJ, Sundaresh V, Wang AT, Erwin PJ, Welt C, Ehrmann D, Montori VM, Murad MH. Adverse effects of the common treatments for polycystic ovary syndrome: a systematic review and meta-analysis. J Clin Endocrinol Metab. 2013 Dec;98(12):4646-54. Electronic copies: Available to subscribers from [The Journal of Clinical Endocrinology & Metabolism \(JCEM\) Web site](#) .
- Domecq JP, Prutsky G, Mullan RJ, Hazem A, Sundaresh V, Elamin MB, Phung OJ, Wang A, Hoeger K, Pasquali R, Erwin P, Bodde A, Montori VM, Murad MH. Lifestyle modification programs in polycystic ovary syndrome: systematic review and meta-analysis. J Clin Endocrinol Metab. 2013 Dec;98(12):4655-63. Electronic copies: Available to subscribers from the [JCEM Web site](#) .

In addition, continuing medical education activities are available in the [original guideline document](#) .

Print copies: Available from The Endocrine Society, Phone: (301) 941.0210; Email: [SocietyServices@endo-society.org](mailto:SocietyServices@endo-society.org)

## Patient Resources

The following are available:

- Polycystic ovary syndrome (PCOS). A patient's guide. Hormone Health Network. 2014 Jan. 2 p. Electronic copies: Available from the [Hormone Health Network Web site](#) .
- Polycystic ovary syndrome (PCOS). 2013 May. Available from the [Hormone Health Network Web site](#) .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

## NGC Status

This NGC summary was completed by ECRI Institute on July 7, 2014. The information was verified by the guideline developer on July 28, 2014. This summary was updated by ECRI Institute on April 15, 2016 following the U.S. Food and Drug Administration advisory on Metformin-containing Drugs.

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